IMMUNOLOGY
FOR MEDICAL STUDENTS

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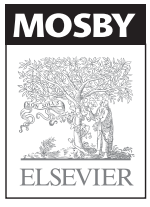
RODERICK NAIRN, PhD
Executive Vice President for Academic Affairs,
Dean, Graduate School of Biomedical Sciences,
Professor, Microbiology & Immunology,
Texas Tech University Health Sciences Center
Lubbock, Texas, USA

MATTHEW HELBERT, MBChB FRCP FRCPath PhD
Consultant Immunologist,
Manchester Royal Infirmary
Manchester, UK

Illustrations by Ethan Danielson



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PREFACE TO THE SECOND EDITION

In preparing this edition, we have made improvements throughout to improve the clarity and accessibility of the material. We have updated all the sections, particularly the material dealing with Toll-like receptors, dendritic cells, regulatory T cells, and HIV. We have also introduced a final chapter on therapeutic immunomodulation, which is being increasingly utilized in clinical practice. This chapter also aims to review what readers will have learned about the immunopathogenesis of several diseases covered in earlier chapters. In response to user feedback, we have also enhanced the clinical vignettes, which form the final pages of most chapters. Although some of these vignettes describe rare diseases, we hope that this helps readers link their studies of immunology with real clinical experience.

PREFACE TO THE FIRST EDITION

We have recognized the need for an immunology book that is primarily focused on the needs of medical students for as long as we have been teachers of immunology. This book has been written to fill this need. Immunology can fall into different medical school courses or modules. Often, the immunology is taught in the Host Defense course, which integrates basic and clinical immunology (including allergy, immunopathology, etc.). Some medical schools, however, teach basic immunology and clinical immunology in two separate courses. This book should be useful for either curriculum organization.

We have concentrated on a simple, straightforward treatment of the subject. The book is relatively short and contains the topics we considered important to understand the human immune system and its role in protecting us from disease. This reflects our acknowledgment of the time constraints on today's medical student. With new topics and a growing amount of information considered to be essential, there are increasing demands on students. It is therefore important to have a concise, readable textbook, and that has been our primary aim. Most chapters contain the information needed for a typical 50-minute large class or small-group teaching/learning session. This, of course, means that details dear to the hearts of some immunologists are not covered!!

We are aware of two specific problems that medical students have with immunology. First, the immune system is complex, because it has evolved to respond to the wide range of pathogens. Many students find themselves bogged down in the complexities of the molecules and cells of the immune system, without having an understanding of how these components work together to fight infection. We begin our book with two overview chapters that explain what the immune system does and then how the components fit together. We recommend that students begin by reading these chapters. Further on in the text, there are more short, integrating overview chapters. These are not just for revision, but are there to make sure that the student understands how the material that they have read fits into the overall system. The second problem is that medical students do not always immediately see the relevance of immunology to day-to-day clinical practice. We have included clinical correlations throughout the text, which explain how understanding the science of immunology can translate into understanding real clinical problems.

The book is a concise description of the science of immunology, a topic that defies a final complete description, because there is much still to be learned. Hopefully, we will have succeeded in inducing an interest and appreciation of the relevance of immunology to medical students, to form the basis for a lifetime of learning about the immune system and its potential for use in improving the human condition. Most medical students today could still be practicing medicine in 40 to 50 years. Approximately 50 years ago, immunology was still in its infancy. For example, we did not know the chemical structure of antibody molecules in any detail, and treatments such as organ transplantation had not been carried out. The next 50 years will likely bring equally important advances in the field. History suggests that we would be foolish to try to predict what they will be. We hope that you enjoy participating in these advances in immunology and their application to human disease as much as we have in those that we have been privileged to observe in our careers.

2002 R.N. & M.H.

ACKNOWLEDGMENTS

Once again I am indebted to my wife, Morag, for her help in preparing my chapters for this book. This edition is dedicated to my family and to all the medical students I have had the opportunity to teach and learn from.

R.N.

My colleagues' generosity has kept me abreast of a rapidly changing subject and provided me with invaluable material for publication. I would not have been able to write this book without the support and patience of my family, to whom I am indebted.

M.H.

HOW TO USE THIS BOOK

Immunology for Medical Students is organized to be read comprehensively. The flow of the book is from genes and molecules to cells and organs, and finally to the immune system as an integrated system protecting the body from infection and helping to maintain the health of the body.

Section 1 introduces the basic concepts and is essential for an understanding of the language of immunology.

Section 2 continues with a discussion of the antigen-recognition molecules, that is, antibodies, T-cell receptors, and the molecules encoded by the major histocompatibility complex.

Section 3 deals with immune physiology, the role of the cells and organs of the immune system in the response to a pathogen.

Section 4 discusses the innate immune system and its connections to the adaptive immune system.

Section 5 considers hypersensitivity, allergy/asthma, autoimmunity, immunodeficiency, transplantation, among others, and includes a new chapter on therapeutic immunomodulation.

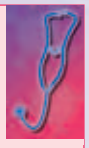
Throughout the book, the core knowledge objectives are listed as Learning Points at the ends of chapters to aid in review. There are also several integrating overview chapters (e.g., Review of antigen recognition, Review of immune physiology), and these focus the student on the major points. Each section is relatively freestanding. For example, Section 5, Immune System in Health and Disease, could be used in a clinical correlations course, independent of the remainder of the book. *Immunology for Medical Students* will be most useful in the comprehensive Host Defense-type courses that are growing in popularity in medical schools.

The icons used throughout are illustrated overleaf. You should become familiar with them immediately to follow the illustrations. We have selected several pathogens (listed in the figure overleaf) to use throughout the book as examples. As a reminder, some basic aspects of the structure and mechanism of action of these organisms are described. You should re-acquaint yourself with these organisms, undoubtedly encountered in microbiology or infectious disease courses, and use the figure as a convenient reference as you encounter these pathogens in the examples in this book.

In general, boxes have been clustered at the end of chapters in the second edition to aid in the flow of the text and in understanding of the material.

CLINICAL BOX

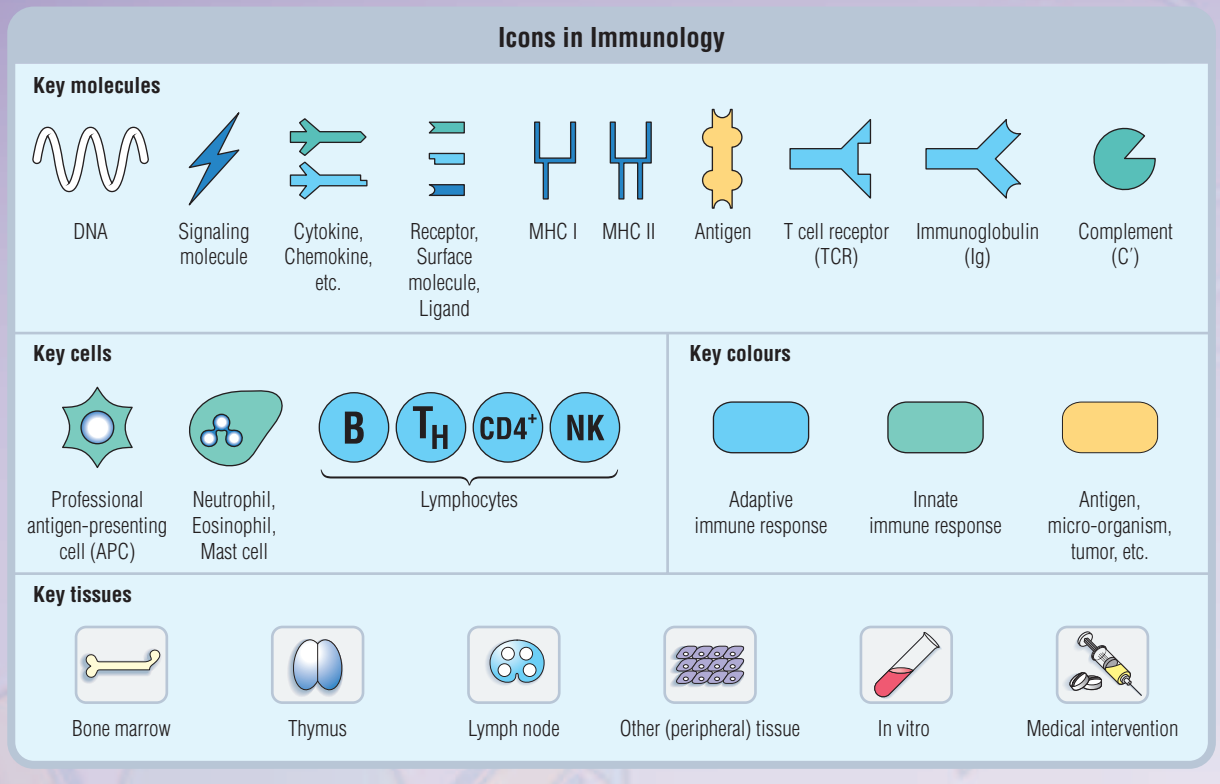
Clinical boxes, throughout the text, put immunology into a clinical context. The clinical material selected is current and relevant.



TECHNICAL BOX

Technical boxes show how advances in the field have expanded our knowledge of how the immune system works, and provided new means of preventing disease.

ICONS


Icons in Immunology
Key molecules
DNA
Signaling molecule
Cytokine, Chemokine, etc.
Receptor, Surface molecule, Ligand
MHC I
MHC II
Antigen
T cell receptor (TCR)
Immunoglobulin (Ig)
Complement (C')
Key cells
Professional antigen-presenting cell (APC)
Neutrophil, Eosinophil, Mast cell
B
TH
CD4+
NK
Lymphocytes
Key colours
Adaptive immune response
Innate immune response
Antigen, micro-organism, tumor, etc.
Key tissues
Bone marrow
Thymus
Lymph node
Other (peripheral) tissue
In vitro
Medical intervention

This figure shows some of the different types of infection the immune system has to cope with. The mechanisms used by the immune system in response to each of these infections is described in detail in different chapters of this book.

Pathogen	Type of Organism	
Human immunodeficiency virus (HIV)	RNA virus	HIV infection requires intimate sexual contact or exposure to blood. HIV has a small genome that frequently mutates, allowing escape from the immune response. Most infected individuals do not develop adequate immunity to clear the virus. Infection frequently results in AIDS. No vaccine exists.
Influenza virus	RNA virus	Influenza causes global epidemics. Casual contact can result in infection of the respiratory tract, causing influenza. Influenza is also a small virus, and annual epidemics reflect the emergence of mutant strains that are not recognized by the populations' immune system. Vaccines exist, but have to be changed every year to overcome mutations. A new avian influenza virus has recently emerged, which would cause a large-scale epidemic if it exchanged genes with the human virus and acquired the ability to easily infect humans.
Epstein-Barr virus (EBV)	DNA virus	EBV infects the pharynx causing glandular fever or "infectious mononucleosis." B lymphocytes of the immune system are also infected, and their uncontrolled growth can sometimes lead to lymphoma (a type of malignancy). EBV has a large genome that does not mutate frequently. The genome encodes proteins that help EBV evade the immune system.
Hepatitis B virus (HBV)	DNA virus	HBV infects liver cells. In many individuals, there is only transient liver damage. In others, there is chronic, severe liver damage, possibly as a result of the immune response to HBV.
Bordetella pertussis	Bacterium	*B. pertussis* infects the airways and causes whooping cough, which can be life-threatening. A very effective vaccine exists, and whooping cough has become rare in the developed world.
Escherichia coli	Bacterium	*E. coli* is a normally harmless bacterium living in the colon. If it enters the bloodstream in small numbers, phagocytes usually destroy such bacteria. When *E. coli* survives in the bloodstream, septic shock may occur.
Mycobacterium tuberculosis	Bacterium	*M. tuberculosis* also infects the airways. It is able to survive inside phagocytes. Because of this intracellular site, it is difficult for the immune system to clear infection, and tuberculosis may result. Tuberculosis is a major threat to global health, in part because patients with AIDS are particularly unable to clear mycobacterial infection.
Schistosoma	Helminth	This worm invades the gut and urinary tract. A special part of the immune system, involving mast cells, has a role in eradicating such infections.

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